

- (b) culturing said epithelial tissue under conditions in which multipotent stem cells proliferate and in which at least 25% of the cells that are not multipotent stem cells die or attach to the culture substrate;
- (c) separating said multipotent stem cells from said cells that attach to said culture substrate; and
- (d) repeating steps (b) and (c) until at least 30% of the cells are multipotent stem cells which are self renewing, form non-adherent clusters, express nestin, and can differentiate into neuronal and mesodermal cell types, or progeny of said multipotent stem cells.

REMARKS

Claims 1-46 constitute the pending claims in the present application. Applicants cancel, without prejudice, claims 35, 45 and 46. Applicants add new claims 47 and 48. Support for the subject matter of these claims is found throughout the specification. No new matter has been entered. Applicants respectfully request reconsideration in view of the following remarks. Issues raised by the Examiner will be addressed below in the order they appear in the prior Office Action.

Formal Matters

Applicants note that claims 18-20, 35 and 43-46 are currently under consideration.

Response to Arguments and Amendment

Applicants note that the amendments and arguments filed 9/21/02 have been entered in full. Applicants note with appreciation that the rejection of claims 18-20 under 35 U.S.C. 112, second paragraph, has been withdrawn. Applicants further note that the rejection of claims 18-20 under 35 U.S.C. 102(b) as being anticipated by Ronnette et al. has been withdrawn.

35 U.S.C. 112, first paragraph

Claim 45 is rejected under 35 U.S.C. 112, first paragraph, as allegedly containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventor had possession of the claimed invention.

Applicants contend that the specification provides ample support for the subject matter of claim 45. The application provides support for the isolation of stem cells from several epithelial tissues including olfactory epithelium, skin and tongue. Furthermore, Applicants remind the Examiner that to satisfy the requirements under 35 U.S.C. 112, first paragraph, Applicants need not recite the claimed subject matter *in haec verba*, using language identical to that provided in the specification as filed. Nevertheless, to expedite prosecution of claims directed to commercially relevant subject matter, Applicants hereby cancel claim 45. Cancellation of claim 45 is not in acquiescence of the rejection, and Applicants reserve the right to prosecute claims of similar or differing scope. Reconsideration and withdrawal of this rejection are respectfully requested.

35 U.S.C. 102(a)

Claims 18-20 and 35 are rejected under 35 U.S.C. 102(a) as allegedly being anticipated by Sosnowski et al. Applicants traverse this rejection to the extent that it is maintained in light of the amended claims.

Applicants reiterate the arguments of record and contend that Sosnowski et al. fail to satisfy the criteria necessary for anticipating the claimed subject matter. In accordance with MPEP 2131 and with the Courts, “a claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference.” *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). “The identical invention must be shown in as complete detail as is contained in the...claim.” *Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989).

Applicants' claims are directed to a method of producing a purified population of multipotent stem cells which are self renewing, form non-adherent clusters, and express nestin. The techniques employed by Sosnowski et al. fail to meet each and every limitation of the pending claims. Most notably, the methods of Sosnowski et al. fail to produce a population of cells which are self renewing, and fail to produce a population of cells which can differentiate into both neuronal and mesodermal cell types, as required by the pending claims. The cells of Sosnowski et al. spontaneously differentiate in culture, and thus can certainly not be considered a self renewing population of cells. That the cells of Sosnowski et al. differentiate to neuronal and glia cells is indicative of just that: the ability of the cells to differentiate to form neurons and glia. This characteristic neither demonstrates nor suggests that the cells are a self-renewing population of cells.

Nevertheless, to expedite prosecution of claims directed to commercially relevant subject matter, Applicants have amended claims 18 and 19 to more explicitly point out that the stem cells are purified from a human. Applicants' amendments are not in acquiescence of the rejection, and Applicants reserve the right to prosecute claims of similar or differing scope.

The teachings of Sosnowski et al. fail to delineate each and every limitation of the pending claims. Sosnowski et al. discloses the isolation of cells from rodent olfactory epithelium. Sosnowski et al. does not disclose the isolation of cells from human olfactory epithelium. Furthermore, Sosnowski et al. fails to teach the isolation of cells from other tissues such as skin or tongue, and Applicants note with appreciation that this rejection was not applied to claims 43 and 44 which explicitly recite that the cells are purified from skin or tongue. Accordingly, the teachings of Sosnowski et al. fail to satisfy the standards required to anticipate the claimed subject matter. Reconsideration and withdrawal of this rejection are respectfully requested.

35 U.S.C. 103(a)

Claims 18-20, 35 and 43-46 are rejected under 35 U.S.C. 103(a) as allegedly being unpatentable over Sosnowski et al. in view of US Patent No. 5,824,489 (the "489 patent").

Applicants traverse this rejection to the extent that it is maintained in light of the amended claims.

Applicants have outlined in detail above why Sosnowski et al. fail to satisfy the criteria necessary to anticipate the claimed subject matter, and the teachings of the '489 patent fail to overcome the deficiencies of Sosnowski et al. The '489 patent discloses the identification and characterization of neural crest stem cells from rats. Although the '489 patent suggests the desirability of identifying and isolating neural crest stem cells from other animals including humans, the mere suggestion of the desirability of isolating human stem cells does not undermine the patentability of the claimed subject matter. One of skill in the art could not have proceeded from the teachings of the '489 patent and arrived at the claimed subject matter with a reasonable expectation of success. Accordingly, the '489 patent fails to overcome the deficiencies of Sosnowski et al. At best, the '489 application provides a motivation for the skilled artisan to undertake the extensive experimentation required to isolate stem cells from humans. The claimed invention may have been obvious to try in light of the prior art, however, obvious to try is distinct from obvious. Reconsideration and withdrawal of this rejection are respectfully requested.

CONCLUSION

In view of the foregoing amendments and remarks, Applicants submit that the pending claims are in condition for allowance. Early and favorable reconsideration is respectfully solicited. The Examiner may address any questions raised by this submission to the undersigned at 617-951-7000. Should an extension of time be required, Applicants hereby petition for same and request that the extension fee and any other fee required for timely consideration of this submission be charged to **Deposit Account No. 18-1945**.

Respectfully Submitted,



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